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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.	
09/977,406	10/15/2001	Seema Garde	CLW 2 0147 4176		
. 7590 07/29/2004			EXAMINER		
Timothy E. Na	· ·	HOLLERAN, ANNE L			
FAY, SHARPE MINNICH & M	•	ART UNIT	PAPER NUMBER		
	Avenue, 7th Floor	1642 DATE MAILED: 07/29/2004			
Cleveland, OH	44114-2516				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary		Application	pplication No. Applicant(s)						
		09/977,406		GARDE ET AL.					
		Examiner		Art Unit					
		Anne Holler		1642					
The MAILING DATE of the Period for Reply	is communication app	ears on the c	over sheet with the c	orrespondence ac	idress				
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.  - Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).  Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).									
Status									
1) Responsive to communic	ation(s) filed on								
2a) ☐ This action is <b>FINAL</b> .	☐ This action is <b>FINAL</b> . 2b) ☐ This action is non-final.								
3) Since this application is in	☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is								
closed in accordance with	closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11, 453 O.G. 213.								
Disposition of Claims									
4)⊠ Claim(s) <u>1-183</u> is/are pen	ding in the application	n.							
4a) Of the above claim(s)	4a) Of the above claim(s) <u>4-64,69-72,77-82,90-156 and 169-174</u> is/are withdrawn from consideration.								
5) Claim(s) is/are allo	5) Claim(s) is/are allowed.								
	6) Claim(s) <u>1-3,65-68,73-76,83-89,157-168 and 175-183</u> is/are rejected.								
7) Claim(s) is/are obj									
8) Claim(s) are subject to restriction and/or election requirement.									
Application Papers									
9)☐ The specification is object	ed to by the Examiner	r.							
10)☐ The drawing(s) filed on is/are: a)☐ accepted or b)☐ objected to by the Examiner.									
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).									
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.									
Tr) The oath or declaration is	objected to by the Ex	aminer. Note	the attached Office	Action or form P	I O-152.				
Priority under 35 U.S.C. § 119									
<ul> <li>12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).</li> <li>a) All b) Some * c) None of:</li> <li>1. Certified copies of the priority documents have been received.</li> <li>2. Certified copies of the priority documents have been received in Application No.</li> <li>3. Copies of the certified copies of the priority documents have been received in this National Stage</li> </ul>									
	International Bureau	-			J				
* See the attached detailed (	Office action for a list of	of the certified	d copies not received	d.					
Attachment(s)		41	Intension: Summer	(DTO 442)					
<ol> <li>Notice of References Cited (PTO-892</li> <li>Notice of Draftsperson's Patent Drawi</li> </ol>			Interview Summary ( Paper No(s)/Mail Da	te					
3) Information Disclosure Statement(s) ( Paper No(s)/Mail Date <u>12/03/2002</u> .			Notice of Informal Pa Other: sequence alignment		D-152)				

Application/Control Number: 09/977,406 Page 2

Art Unit: 1642

## **DETAILED ACTION**

1. The preliminary amendment received March 28, 2002 is acknowledged. Claims 96-183 were added. Claims 1-183 are pending.

2. Prior to setting forth the restriction requirement, it is noted that the claims recite improper Markush Groups. M.P.E.P. 803.02 states that: Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978); and *In re Haas*, 580 F.2d 461,198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, *unless the subject matter in a claim lacks unity of invention* [emphasis added], *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility. In the instant case, each of the products is a separate and distinct polypeptide, which differs in structure from any of the other polypeptide products to such an extent that non-coextensive searches are required. As such, the structurally different polypeptide products have been restricted each from the other.

#### Election/Restrictions

- 3. Restriction to one of the following inventions is required under 35 U.S.C. 121:
  - I. Claims 1-3, 65-68, 71-76, 83-89, 157-168, and 175-183 drawn to peptides, peptide analogs, and pharmaceutical compositions thereof, to the extent the peptides comprise SEQ ID NO:3, and to the extent the peptide analogs comprise 5

amino acids or 2 amino acids of SEQ ID NO: 3, classified in classes 530, 424, and 514 subclasses 300, 184.1, and 2, respectively.

- II. Claims 1-3, 65-68, 71-76, 83-89, 157-168, and 175-183 drawn to peptides, peptide analogs, and pharmaceutical compositions thereof, to the extent the peptides comprise SEQ ID NO:4, and to the extent the peptide analogs comprise 5 amino acids or 2 amino acids of SEQ ID NO: 4, classified in classes 530, 424, and 514 subclasses 300, 184.1, and 2, respectively.
- III. Claims 1-3, 65-68, 71-76, 83-89, 157-168, and 175-183 drawn to peptides, peptide analogs, and pharmaceutical compositions thereof, to the extent the peptides comprise SEQ ID NO:5, and to the extent the peptide analogs are peptide analogs of SEQ ID NO: 5 (SEQ ID NOs: 59-88, SEQ ID Nos 10-58, amino acid fragments of SEQ ID NO: 5, analogs having either 50, 70 or 90% identity to SEQ ID NO: 5, classified in classes 530, 424, and 514 subclasses 300, 184.1, and 2, respectively.
- IV. Claims 1-3, 65-68, 71-76, 83-89, 157-168, and 175-183 drawn to peptides, peptide analogs, and pharmaceutical compositions thereof, to the extent the peptides comprise SEQ ID NO: 6, and to the extent the peptide analogs comprise 5 amino acids or 2 amino acids of SEQ ID NO: 6, classified in classes 530, 424, and 514 subclasses 300, 184.1, and 2.
- V. Claims 2-3, 83-89, and 175-183 drawn to peptide analogs and pharmaceutical compositions thereof, peptides, to the extent the peptide analogs comprise SEQ
   ID NO: 89, classified in classes 530, 424, and 514 subclasses 300, 184.1, and 2.

- VI. Claims 2-3, 65-72, 74-76, 83-89, 145-156, 160-168, and 175-183 drawn to peptides, peptide analogs, and pharmaceutical compositions thereof, to the extent the peptides comprise SEQ ID NO:2, and to the extent the peptide analogs comprise 5 amino acids or 2 amino acids of SEQ ID NO: 2, classified in classes 530, 424, and 514 subclasses 300, 184.1, and 2, respectively.
- VII. Claims 77-82, and 169-174 drawn to pharmaceutical compositions comprising vectors or polynucleotides comprising SEQ ID NO: 9, classified in class 514, subclass 44.
- VIIIa. Claims 4-9, 11-33, 35-42, 55-64, 90-99, 101-128 and 137-144 drawn to methods of treatment of **prostatic cancer** comprising the use or administration of **SEQ ID**NO: 2, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- VIIIb. Claims 4-9, 11-33, 35-42, 55-64, 90-99, 101-128 and 137-144 drawn to methods of treatment of stomach cancer comprising the use or administration of SEQ ID
  NO: 2, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- VIIIc. Claims 4-9, 11-33, 35-42, 55-64, 90-99, 101-128 and 137-144 drawn to methods of treatment of breast cancer comprising the use or administration of SEQ ID
  NO: 2, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- VIIId. Claims 4-9, 11-33, 35-42, 55-64, 90-99, 101-128 and 137-144 drawn to methods of treatment of **endometrial cancer** comprising the use or administration of **SEQ**

Art Unit: 1642

ID NO: 2, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.

Page 5

- VIIIe. Claims 4-9, 11-33, 35-42, 55-64, 90-99, 101-128 and 137-144 drawn to methods of treatment of **ovarian cancer** comprising the use or administration of **SEQ ID**NO: 2, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- VIIIf. Claims 4-9, 11-33, 35-42, 55-64, 90-99, 101-128 and 137-144 drawn to methods of treatment of **benign prostatic hyperplasia** comprising the use or administration of **SEQ ID NO: 2, or analogs thereof**, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- IXa. Claims 4, 5, 10-30, 34-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of **prostatic cancer** comprising the use or administration of **SEQ ID**NO: 3, or analogs, thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- IXb. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of stomach cancer comprising the use or administration of SEQ ID NO: 3, or analogs, thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- IXc. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of breast cancer comprising the use or administration of SEQ ID NO: 3, or analogs, thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.

- IXd. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of endometrial cancer comprising the use or administration of SEQ ID NO: 3, or analogs, thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- IXe. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of **ovarian cancer** comprising the use or administration of **SEQ ID NO: 3, or analogs, thereof**, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- IXf. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of benign prostatic hyperplasia comprising the use or administration of SEQ ID NO: 3, or analogs, thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- Xa. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of **prostatic cancer** comprising the use or administration of **SEQ ID NO: 4, or analogs thereof**, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- Xb. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of stomach cancer comprising the use or administration of SEQ ID NO: 4, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- Xc. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of breast cancer comprising the use or administration of SEQ ID NO: 4, or

Art Unit: 1642

analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.

Page 7

- Xd. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of endometrial cancer comprising the use or administration of SEQ ID NO: 4, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- Xe. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of ovarian cancer comprising the use or administration of SEQ ID NO: 4, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- Xf. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of benign prostatic hyperplasia comprising the use or administration of SEQ ID
  NO: 4, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- XIa. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of prostatic cancer comprising the use or administration of SEQ ID NO: 5, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- XIb. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of stomach cancer comprising the use or administration of SEQ ID NO: 5, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.

- XIc. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of breast cancer comprising the use or administration of SEQ ID NO: 5, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- XId. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of endometrial cancer comprising the use or administration of SEQ ID NO: 5, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- XIe. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of **ovarian cancer** comprising the use or administration of **SEQ ID NO: 5, or analogs thereof**, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- XIf. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of benign prostatic hyperplasia comprising the use or administration of SEQ ID NO: 5, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- XIIa. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of prostatic cancer comprising the use or administration of SEQ ID NO: 6, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- XIIb. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of stomach cancer comprising the use or administration of SEQ ID NO: 6, or

- analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- XIIc. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of breast cancer comprising the use or administration of SEQ ID NO: 6, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- XIId. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of endometrial cancer comprising the use or administration of SEQ ID NO: 6, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- XIIe. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of **ovarian cancer** comprising the use or administration of **SEQ ID NO: 6, or analogs thereof**, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- XIIf. Claims 4-42, 55-64, 90-95, 100-128 and 137-144 drawn to methods of treatment of benign prostatic hyperplasia comprising the use or administration of SEQ ID NO: 6, or analogs thereof, classified in classes 424 and 514 subclasses 184.1, 185.1 and 2, respectively.
- XIIIa. Claims 43-64 and 129-136 drawn to methods of treatment of **prostatic cancer** comprising the use or administration of **SEQ ID NO: 9**, thereof, classified in class 514, subclass 44.

- XIIIb. Claims 43-64 and 129-136 drawn to methods of treatment of **stomach cancer** comprising the use or administration of **SEQ ID NO: 9,** classified in class 514, subclass 44.
- XIIIc. Claims 43-64 and 129-136 drawn to methods of treatment of breast cancer comprising the use or administration of SEQ ID NO: 9, classified in class 514, subclass 44.
- XIIId. Claims 43-64 and 129-136 drawn to methods of treatment of **endometrial cancer** comprising the use or administration of **SEQ ID NO: 9,** classified in class 514, subclass 44.
- XIIIe. Claims 43-64 and 129-136 drawn to methods of treatment of **ovarian cancer** comprising the use or administration of **SEQ ID NO: 9,** classified in class 514, subclass 44.
- XIIIf. Claims 43-64 and 129-136 drawn to methods of treatment of benign prostatic hyperplasia comprising the use or administration of SEQ ID NO: 9, classified in class 514, subclass 44.
- 4. The inventions are distinct, each from the other, for the following reasons:
- A. Claims 65-68 and 74-76 link inventions I-IV and VI. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claims, claims 65-68 and 74-76. Claims 65-68 and 74-76 link inventions I-IV because the claimed inventions read on pharmaceutical compositions that are mixtures of each of the separate polypeptides or peptide analogs. Upon the allowance of the linking claims, the restriction requirement as to the linked

inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination in the instant application. Applicant is advised that if any such claims depending from or including all the limitations of the allowable linking claims are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims in the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

B. Claims 4, 5, 19, 20, 29, 30, 55, 56, 91, 92 and 95 link inventions VIIIa-VIIIf. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claims, claims 4, 5, 19, 20, 29, 30, 55, 56, 91, 92 and 95. Claims 4, 5, 19, 20, 29, 30, 55, 56, 91, 92 and 95 link inventions VIIIa-VIIIf, because the claimed inventions read on methods of generically treating cancers of epithelial secretion, or inhibiting the growth of tumors, or treating diseases characterized by elevated levels of FSH. Upon the allowance of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination in the instant application. Applicant is advised that if any such claims depending from or including all the limitations of the allowable linking claims are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims in the instant application. Where a restriction requirement is withdrawn, the provisions of

35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

- C. Claims 4, 5, 19, 20, 29, 30, 55, 56, 91, 92 and 95 link inventions IXa-IXf. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claims, claims 4, 5, 19, 20, 29, 30, 55, 56, 91, 92 and 95. Claims 4, 5, 19, 20, 29, 30, 55, 56, 91, 92 and 95 link inventions IXa-IXf, because the claimed inventions read on methods of generically treating cancers of epithelial secretion, or inhibiting the growth of tumors, or treating diseases characterized by elevated levels of FSH. Upon the allowance of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination in the instant application. Applicant is advised that if any such claims depending from or including all the limitations of the allowable linking claims are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims in the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. In re Ziegler, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.
- D. Claims 4, 5, 19, 20, 29, 30, 55, 56, 91, 92 and 95 link inventions Xa-Xf. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claims, claims 4, 5, 19, 20, 29, 30, 55, 56, 91, 92 and 95. Claims 4, 5, 19, 20, 29, 30, 55, 56, 91, 92 and 95 link inventions Xa-Xf, because the claimed inventions read on methods of generically treating cancers of epithelial secretion, or inhibiting the growth of tumors, or treating

Art Unit: 1642

diseases characterized by elevated levels of FSH. Upon the allowance of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination in the instant application. Applicant is advised that if any such claims depending from or including all the limitations of the allowable linking claims are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims in the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Page 13

E. Claims 4, 5, 19, 20, 29, 30, 55, 56, 91, 92 and 95 link inventions XIa-XIf. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claims, claims 4, 5, 19, 20, 29, 30, 55, 56, 91, 92 and 95. Claims 4, 5, 19, 20, 29, 30, 55, 56, 91, 92 and 95 link inventions XIa-XIf, because the claimed inventions read on methods of generically treating cancers of epithelial secretion, or inhibiting the growth of tumors, or treating diseases characterized by elevated levels of FSH. Upon the allowance of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination in the instant application. Applicant is advised that if any such claims depending from or including all the limitations of the allowable linking claims are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the

Art Unit: 1642

claims in the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. In re Ziegler, 44 F.2d 1211, 1215, 170 USPO 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Page 14

- F. Claims 4, 5, 19, 20, 29, 30, 55, 56, 91, 92 and 95 link inventions XIIa-XIIf. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claims, claims 4, 5, 19, 20, 29, 30, 55, 56, 91, 92 and 95. Claims 4, 5, 19, 20, 29, 30, 55, 56, 91, 92 and 95 link inventions XIIa-XIIf, because the claimed inventions read on methods of generically treating cancers of epithelial secretion, or inhibiting the growth of tumors, or treating diseases characterized by elevated levels of FSH. Upon the allowance of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination in the instant application. Applicant is advised that if any such claims depending from or including all the limitations of the allowable linking claims are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims in the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. In re Ziegler, 44 F.2d 1211, 1215, 170 USPO 129, 131-32 (CCPA 1971). See also MPEP § 804.01.
- G. Claims 43 and 44 link inventions XIIIa-XIIIf. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claims, claims 43 and 44. Claims 43 and 44 link inventions XIIIa-XIIIf, because the claimed inventions read on methods of generically treating cancers of epithelial secretion, or inhibiting the growth of

Page 15

Art Unit: 1642

tumors. Upon the allowance of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination in the instant application. Applicant is advised that if any such claims depending from or including all the limitations of the allowable linking claims are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims in the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Inventions I-VI are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions, are drawn to structurally different polypeptide products, and in the case of invention group VI, drawn to a polynucleotide product. Therefore, where structural identity is required, such as for making antibodies to each of the polypeptide products, the individual polypeptides have different effects. In the case of the polynucleotide product of group VI, the uses of polynucleotides are entirely different and separate from the uses of polypeptides. For example, polynucleotides can be used to make polypeptide products or in methods of nucleic acid hybridization, whereas polypeptide products are used in methods to make antibodies.

Application/Control Number: 09/977,406 Page 16

Art Unit: 1642

products.

6. The methods of Inventions VIIIa-VIIIf, IXa-IXf, Xa-Xf, XIa-XIf, XIIa –XIIf, and XIIIa-XIIIf differ in the method objectives, and in patient population treated and product used in the claimed methods. The different inventions are drawn to methods of treating different diseases, some having to do with cancer, others benign diseases; and the different inventions differ in product that makes up the pharmaceutical composition useful for treating each of the separate diseases. The diseases comprise 6 different diseases and the products comprise 6 different, structurally distinct products. In the case of the inventions of group XIII, the products are polynucleotide products, and thus, the inventions read on gene therapy methods, whereas all the other invention groups are drawn to methods comprising the administration of polypeptide

- 7. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.
- 8. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection

Application/Control Number: 09/977,406 Page 17

Art Unit: 1642

are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**.

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

9. During a telephone conversation with Tim Nauman on or about March 9, 2004 a provisional election was made with traverse to prosecute the invention of Group III, claims 1-3, 65-68, 71-76, 83-89, 157-168 and 175-183, to the extent the claims read on SEQ ID NO: 5 and

analogs of SEQ ID NO: 5, and pharmaceutical compositions comprising SEQ ID NO: 5 and analogs of SEQ ID NO: 5. Affirmation of this election must be made by applicant in replying to this Office action. Claims 4-64, 69-72 (claims 71 and 72 do not contain a reference to SEQ ID NO: 5), 90-156 and 169-174 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

- 10. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).
- 11. Claims 1-183 are pending.

Claims 4-64, 69, 70-72, 77-82, 90-156, and 169-174, drawn to non-elected inventions, are withdrawn from consideration. Claims 71 and 72 do not contain a recitation concerning a limitation of a polypeptide comprising SEQ ID NO: 5.

Claims 1-3, 65-68, 73-76, 83-89, 157-168 and 175-183, to the extent they read on SEQ ID NO: 5 and variants thereof, are examined on the merits.

12. Claims 2, 3, 65-68, 73-76, 83-89, 157-168, and 175-183 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 3, 83-86 is indefinite because of the phrases "two to fifty units of SEQ ID NO: 5", "two to ten units of SEQ ID NO: 5" and "two to fourteen amino acid units of SEQ ID NO: 5". If "units" is meant to refer to "amino acids", then the claims should be amended to recite this. Furthermore, SEQ ID NO: 5 is 15 amino acids in length, thus, the phrase "two to fifty units" does not make sense.

Claim 65-68 is indefinite because it is not clear if the claim is drawn to a polypeptide that consists of SEQ ID NO: 5 (the peptide consisting of PCK3145) or if the polypeptide comprises SEQ ID NO: 5. For the purposes of comparison with the art, claim 65 is interpreted to be drawn to a pharmaceutical composition comprising a polypeptide comprising SEQ ID NO: 5.

Claims 75, 88, 161-163, and 176-178 are indefinite because of the phrase "taxol derivative". The metes and bounds of the claims cannot be determined because a closed definition of the term "taxol derivative" is not present in the text. The term "derivative" may encompass compounds that have in common as little as one molecule of the parent molecule.

13. Claims 2, 3, 83-89, and 175-183 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polypeptides comprising SEQ ID NO: 5, does not reasonably provide enablement for polypeptides that consist of variants of SEQ ID NO: 5 or that comprise a sequence that is a variant of SEQ ID NO: 5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation

necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The claimed inventions encompass polypeptides and pharmaceutical compositions comprising said polypeptides, where the polypeptides are sequence variants of a polypeptide consisting of SEQ ID NO: 5, which appears to be identified in the specification as peptide "PCK3145". The variants may have as little in common with SEQ ID NO: 5 as only 2 amino acids or the variants may be defined as having 50%, 70% or 90% sequence identity with SEQ ID NO: 5. The claimed inventions encompass those polypeptides that are capable of inhibiting the growth of prostatic adenocarcinoma, stomach cancer, breast cancer, endometrial cancer, ovarian or other epithelial cancers or of benign prostatic hyperplasia. However, the specification limits its teachings to the efficacy of PCK3145 in inhibiting the growth of prostate cancer cells and in inducing apoptosis in prostate cancer cells.

The disclosure does not contain an adequate written description, examples, or guidance by which the claimed variants could be placed into the hands of the skilled artisan with a reasonable expectation of success without requiring undue experimentation for the following reasons. There is no evidence in the specification that any variants of SEQ ID NO:5 have activity on prostate cancer cells, let alone the ability to inhibit the growth of stomach cancer, breast cancer, endometrial cancer, ovarian or other epithelial cancers or of benign prostatic hyperplasia. Furthermore, the relationship between the primary amino acid sequence and protein function is highly unpredictable. Bowie et al (Science, 247: 1306-1310, 1990) teaches that while

it is known that many amino acid substitutions are possible in any given protein, the position with the protein sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Burgess et al (J. Cell Biology, 111: 2129-2138, 1990) teaches that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Lazar et al (Molecular and Cellular Biology, 8: 1247-1252, 1988) teaches that replacement of aspartic acid at position 47 with alanine or asparagines does not affect biological activity while replacement with serine or glutamic acid sharply reduces the biological activity of the protein. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. Because of the unpredictability of the protein arts, and because of the lack of teachings directed to the biological activity of any of the claimed variants and the lack of teachings directed to the biological activity of SEQ ID NO: 5 or any of its variants with respect to the ability to inhibit the growth of stomach cancer, breast cancer, endometrial cancer, ovarian or other epithelial cancers or of benign prostatic hyperplasia, the skilled artisan cannot make and use the broad genus of variants recited in the claims. The disclosure does not adequately describe, provide guidance or give examples of the critical amino acid residues that bestow upon the protein its desired characteristics.

The claimed inventions encompass a broad genus of polypeptide variants of polypeptides comprising the amino acid sequence of SEQ ID NO: 5. The working embodiments of the specification are a minor portion of a very broad genus (SEQ ID NO: 5 itself) and do not teach or support the majority of the genus as a whole. Additionally, some of the variants have so little in

common with SEQ ID NO: 5 (e.g. comprising 2 amino acids or having 50% sequence identity) that the claimed inventions are essentially drawn to polypeptides limited by what they do and not by what they are. Such a broad and varied genus drawn to the biological functionality of the product used without regard or limitation to its chemical structure cannot be adequately enabled from the few examples taught, especially in light of the fact that not all of the functionalities are taught (i.e. inhibition of stomach cancer, breast cancer, endometrial cancer, ovarian or other epithelial cancers or of benign prostatic hyperplasia).

14. Claims 75, 88, 161-163, and 176-178 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that disclosure does not adequately describe the genus of "taxol derivatives".

The scope of the term "derivative" has not been described in the specification, and therefore, encompasses compounds that have in common with taxol as little a one molecule (comprise one molecule). Therefore, the scope of the genus of "taxol derivatives" is not adequately described, because the two examples of taxol derivatives provided, taxotere and taxane, are not representative of the full scope of the genus of taxol derivatives. Without a representative number of embodiments of a genus, the structures of genus cannot be envisioned by one of skill in the art. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making or testing it. One

cannot describe what one has not conceived. See Fides v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112, is severable from its enablement provision. (See page 1115).

Page 23

15. Claims 2, 3, 83-89, and 175-183 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that disclosure does not adequately describe the genus of polypeptides that are structural variants of SEQ ID NO: 5.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is for purposes of the 'written description' inquiry, "whatever is now claimed" (see page 1117). The specification does not "clearly allow persons" of ordinary skill in the art to recognize that [he or she] invented what is now claimed." (See Vas-Cath at page 1116.)

The claimed inventions are drawn to polypeptides and pharmaceutical compositions comprising polypeptides, where the polypeptides may have very little in common structurally with SEQ ID NO: 5, which is a polypeptide that is provided by the disclosure of the specification and which is a polypeptide that the disclosure teaches has apoptosis-inducing activity in PC-3

Application/Control Number: 09/977,406 Page 24

Art Unit: 1642

cells (a prostate adenocarcinoma cell line), growth inhibitory activity in PC-3 cells, inhibits the growth of prostate cancer cell xenografts in nude mice, and inhibits the growth of rat prostate tumors in Dunning rats and also in Copenhagen rats. The specification does not provide any teachings demonstrating that any variants of SEQ ID NO: 5 have similar biological functions, and fails to teach which structural feature of SEQ ID NO: 5 confers the observed biological activity of SEQ ID NO: 5.

The variants are polypeptides such as polypeptides that comprises at least two contiguous amino acids of SEQ ID NO: 5; comprises at least five contiguous amino acids of SEQ ID NO: 5; comprises between two to 15 amino acids of SEQ ID NO: 5 (within two to fifty "units"); comprises between two to ten amino acids of SEQ ID NO: 5 (two to ten "units"); comprises between two to fourteen amino acid units of SEQ ID NO: 5; comprises a polypeptide having at least 90% of its amino acid sequence identical to the amino acid sequence set forth in SEO ID NO: 5; comprises a polypeptide having at least 70% of its amino acid sequence identical to the amino acid sequence set forth in SEQ ID NO: 5; and comprises a polypeptide having at least 50% of its amino acid sequence identical to the amino acid sequence set forth in SEQ ID NO: 5; where the variants have the biological activity of inhibiting the growth of prostate cancer cells or of causing apoptosis in prostate cancer cells. Furthermore, the claims are drawn to polypeptides and pharmaceutical compositions comprising polypeptides, where the polypeptides are capable of inhibiting the growth of stomach cancer, breast cancer, endometrial cancer ovarian cancer or other epithelial cancers, or of inhibiting benign prostate hyperplasia. The specification contains no teachings that SEQ ID NO: 5 has this ability let alone any variants of SEQ ID NO: 5.

Because the specification fails to teach the part or parts of SEQ ID NO: 5 that confer biological activity upon the amino acid sequence of SEQ ID NO: 5, and because the specification confines its teachings of biological activity to the induction of apoptosis of prostatic cancer cells, and because the claims are broadly drawn to structures that have as little in common with SEQ ID NO: 5 as two contiguous amino acids, the claimed variants are equivalent to claims reciting only functional limitations (i.e. claiming a compound by what it does and not by what it is). In the case of claiming by functional limitations, one of skill in the art cannot conceive of the structures of a representative number of examples of variants that fall within the claimed genus of polypeptide variants. Therefore conception of the genus is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of manufacturing or testing the claimed variants for the desired activity. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making or testing it. One cannot describe what one has not conceived. See Fides v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Applicant is reminded that <u>Vas-Cath</u> makes clear that the written description provision of 35 U.S.C. 112, is severable from its enablement provision. (See page 1115).

### Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

Application/Control Number: 09/977,406 Page 26

Art Unit: 1642

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1-3, 65-68, 73-76, 83-89, 157-168, and 175-183 are rejected under 35 U.S.C. 102(b) as being anticipated by Sheth (U.S. Patent 5,48,011; issued June 27, 1995; cited in the IDS).

The claims are drawn to polypeptides and to pharmaceutical compositions comprising the polypeptides. The pharmaceutical compositions may also include anticancer drugs. The polypeptides comprise SEQ ID NO: 5 or variants of SEQ ID NO: 5. In the cases where the claims recite "as set forth in SEQ ID NO: 5", the claims are interpreted to read on polypeptides that comprise, at a minimum, the amino acid sequence of SEQ ID NO: 5, because the claims do not contain the transitional phrases "consisting of" or "comprising". In the absence of these phrases, the claims are interpreted broadly as if the transitional phrase "comprising" were present in the claims.

Sheth teaches the polypeptide, HSPI, which comprises 94 amino acids (SEQ ID NO: 1) that comprises the amino acid sequence of SEQ ID NO: 5 of the instant application. Sheth also teaches pharmaceutical compositions comprising HSPI, where the HSPI is present in the dosage range of about 5 ng/kg/day to about 10 ug/kg/day (col. 2, lines 42-47). Sheth further teaches compositions where the HSPI is combined with anticancer drugs such as idarubicin, adriamycin, doxorubicin and daunomycin (col. 9, lines 57-65). Sheth teaches that therapeutic polypeptides may be encapsulated and delivered using slow release technology comprising a liposome delivery system or polysaccharides (col. 9, lines 14-21). Sheth teaches that HSPI is cytotoxic to

gastric cancer cells (col. 9, line 66 – col. 10, line 18) and inhibits the growth of adenocarcinoma of the prostate (col. 7, lines 16-53).

The HSPI polypeptide of Sheth anticipates the claimed inventions because HSPI comprises SEQ ID NO: 5; comprises at least two contiguous amino acids of SEQ ID NO: 5; comprises at least five contiguous amino acids of SEQ ID NO: 5; comprises SEQ ID NO: 88; comprises SEQ ID NO: 58; comprises between two to 15 amino acids of SEQ ID NO: 5 (within two to fifty "units"); comprises between two to ten amino acids of SEQ ID NO: 5 (two to ten "units"); comprises between two to fourteen amino acid units of SEQ ID NO: 5; comprises a polypeptide having at least 90% of its amino acid sequence identical to the amino acid sequence set forth in SEQ ID NO: 5; comprises a polypeptide having at least 70% of its amino acid sequence identical to the amino acid sequence set forth in SEQ ID NO: 5; and comprises a polypeptide having at least 50% of its amino acid sequence identical to the amino acid sequence set forth in SEQ ID NO: 5. Therefore, Sheth teaches polypeptides and pharmaceutical compositions that are the same as that claimed.

17. Claims 2, 3, 84, and 86 are rejected under 35 U.S.C. 102(e) as being anticipated by Tsai (U.S. Patent 5,994,298; issued Nov. 30, 1999; effective filing date Sep. 8, 1998) as evidenced by Tracey (U.S. Patent 6,319,894; issued Nov. 20, 2001).

Tsai teaches and claims methods of inducing apoptosis in cancer cells comprising administering fetuin. Fetuin is a protein that comprises at least 2 contiguous amino acids from the amino acid sequence of SEQ ID NO: 5 ("Cys Thr" at positions amino acids 248-249 of SEQ ID NO: 1), as evidenced by Tracey, which provides a sequence of human fetuin (see col. 2, lines

25-42). Tsai teaches that apoptosis proteins (e.g. fetuin) may be a new class of anticancer drugs (col. 2, lines 16-21; col. 5, line 48 – col. 7, lines 33; col. 16, lines 1-4; col. 18, lines 3-22). Thus, Tsai teaches polypeptides and pharmaceutical compositions that are the same as that claimed.

18. Claims 2 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Nolet (Nolet, S. et al., Biochimica et Biohysica Acta, 1089: 247-249, 1991).

Claims 2 and 3 encompass variants comprising an amino acid sequence that has at least 50 % or 70% sequence identity to SEQ ID NO: 5.

Nolet teaches PSP<sub>94</sub> isolated from Rhesus monkeys, which has an amino acid sequence comprising a sequence that has 81.4% sequence identity to SEQ ID NO: 5 (see enclosed alignment). Because Nolet teaches that this a PSP<sub>94</sub> protein from Rhesus monkey, absent evidence to the contrary, this sequence is assumed to have the same function as the human PSP<sub>94</sub>. Therefore, Nolet teaches polypeptides that are the same as that claimed.

19. Claims 2 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Xuan (Xuan, J.W. et al., DNA & Cell Biology, 16: 627-638, 1997).

Claims 2 and 3 encompass variants comprising an amino acid sequence comprising at least 5 contiguous amino acids from SEQ ID NO: 5.

Xuan teaches a PSP<sub>94</sub> isolated from baboon, which has an amino acid sequence that comprises 6 amino acids of SEQ ID NO: 5 (see enclosed alignment). Because Xuan teaches that this a PSP<sub>94</sub> protein from baboon, absent evidence to the contrary, this sequence is assumed to

have the same function as the human PSP<sub>94</sub>. Therefore, Xuan teaches polypeptides that are the same as that claimed.

## Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

Anne L. Holleran Patent Examiner July 22, 2004

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

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page
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N,Alternate names: prostatic secretory protein PSP94
C;Species: Macaca mulatta (rhesus macaque)
C;Date: 02-Jun-1995 #sequence revision 02-Jun-1995 #text_change 20-Aug-1999
C;Accession: 916237; A54663
C;Accession: 916237; A54663
R;Nolet, S.; Mbikay, M.; Chretien, M.
Biochim. Biophys. Acta 1089, 247-249, 1991
A;Ritle: Prostatic secretory protein PSP(94): gene organization and promoter A;Reference number: S16237; MUID:91244357; PMID:2054385
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A;Molecule type: DNA
A;Residues: 1-114 <NO2>
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Cancer Lett. 74, 91-99, 1993
A;Title: Decreased expression of prostatic secretory protein
A;Reference number: I52682; MUID:94115955; PMID:7506990
A;Accession: I52682
A;Status: preliminary; translated from GB/EMBL/DDBJ
                                                                hypothetical
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C;Superfamily: seminal plasma protein
F;1-20/Domain: signal sequence #status predicted <SIG>
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A;Map position: 10q11.2-10q11.2
A;Introns: 1/3; 37/1; 72/2
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;Comment: This protein is a component of seminal plasma as well as secr
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C;Laccession: S41663
C;Accession: S41663
R;Pernlund, P.; Granberg, L.B.; KUEFFE
R;Pernlund, P.; Granberg, L.B.; KUEFFE
Arch. Biochem. Biophys. 309, 70-76, 1994
                                                                                                                                                       beta-microseminoprotein - pig
C;Species: Sus scrofa domestica (domestic pig)
C;Date: 19-Mar-1997 #sequence_revision 19-Mar-1997
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C;Species: Caenorhabditis elegans
-C;Date: 15-Oct-1999 #sequence_revision 15-Oct-1999 #text_change 15-Oct-1999
C;Accession: T18649
R;McMurray, A.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              RESULT 4
S63986
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                submitted to the EMBL Data Library, A;Reference number: Z19001 A;Accession: T18649
                                                                                                                                                            C;Keywords: extraceilliar maria.
F;15-73/Domain: von Willebrand factor type C repeat homology <VWC>
                                                                                                                                                                                                    A;Introns: 73/1; 136/2; 221/1; 369/1; 517/1; 659/1; 799/1; 948/1; 1093/1; 1236/1
C;Superfamily: von Willebrand factor type C repeat homology
C;Keywords: extracellular matrix
                                                                                                                                                                                                                                                                                                                                                                                                                                                          R;Exposito,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        R;Exposito, J.Y; Boute, N; Deleage, G.; Garrone, R.
Eur. J. Biochem. 234, 59-65, 1995
A;Title: Characterization of two genes coding for a similar four-cysteine motif of the A;Reference number: S63985; MUID:96096722; PMID:8529669
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 C;Species: Strongylocentrotus purpuratus (purple urchin)
C;Date: 20-Jul-1996 #sequence_revision 08-Nov-1996 #text_change 25-Apr-1997
C;Accession: S63986; S64638
                                                                                                                                                                                                                                                                                                                                                                                                             submitted to the EMBL Data Library, July 1995
A;Reference number: S64637
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      collagen alpha 5 chain - sea urchin (Strongylocentrotus purpuratus) (fragment)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         A; Introns: 46/3; 84/1; 212/1; 307/2; 345/2; 394/1; 424/2; 481/1;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 A; Map position: 5
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   A; Experimental source: clone
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     A;Molecule type: DNA
A;Residues: 1-884 <W
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           A;Status: preliminary; translated from GB/EMBL/DDBJ
                                                                                                                                                                                                                                                                      A;Gene: COLPSalpha
                                                                                                                                                                                                                                                                                                                 A;Residues: 1-658,'G',660-870,'G',872-901,'H',903-1185,'T',1187-1214,'Y',1216-1376 <EX
A;Cross-references: EMBL:X89804
                                                                                                                                                                                                                                                                                                                                                                A; Molecule type: DNA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                               A;Cross-references: EMBL:X89804
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       A;Residues:
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                                                                                                                                                                                                                                                                                                                                                                                          A;Accession:
                                                                                         Matches
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                                                                                                               Best Local
                                                                                                                                    Query Match
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                                                                                                            Similarity
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EWKVDECTTCAC
                                          EWQTDNCETCTC 12
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                                                                                                            Score 54; I
Pred. No. 9.
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                                                                                         Mismatches
                                                                                                                                    DB 2;
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#text\_change 31-Oct-1997

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porcine seminal plasma

PREPARED AND PRESENTATION OF THE PRESENTATION

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RESULT 3
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Best Local Similarity
Matches 15; Conser
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                                                                                                                                                                                                                                                                                                                                                                                                                                      Signal.
SIGNAL
CHAIN
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           secretory protein of 94 amino acids) in primates.";
DNA Cell Biol. 16:627-638(1997).
-I- FUNCTION: Inhibits the secretion of secretion of secretion of secretion of secretion.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       EMBL; U49786; AAB62726.1; -. InterPro; IPR008735; PSP94.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   01-NOV-1997 (Rel. 35, Created)
01-NOV-1997 (Rel. 35, Last sequence update)
28-FEB-2003 (Rel. 41, Last annotation update)
Beta-microseminoprotein precursor (Prostate secreted seminal plasma protein) (Prostate secretory protein PSP94) (PSP-94)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Pfam; PF05825; PSP94; 1.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             This SWISS-PROT entry is copyright. It is produced through between the Swiss Institute of Bioinformatics and the EN
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  MEDLINE=97316893; PubMed=9174167; Xuan J.W., Wu D., Guo Y., Garde S
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Cercopithecidae;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           PAPAN
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                                                                                                                                                                                                                   Similarity 7; Conserv
                                                                                                                                                                        WOTDNCE 8
                                                                                                                             WOTDNEE 58
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                                                                                                                                                                                                                                  Score 7;
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BETA-MICROSEMINOPROTEIN
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OR 70 (BY SIMILARITY).
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Pred. No. 6.9e-12
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MBL outstation -
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BINDING
BINDING
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Sieker L., LeGall J., Carrondo M.A.;
Sieker L., LeGall J., Carrondo M.A.;
"The primary and three-dimensional structures of a nine-haem
"The primary and three-dimensional structures of a new description of the Hmc family.";
Structure 7:119-130(1999).

Structure 7:119-130(1999).

-I- FUNCTION: MAY FORM PART OF A TRANSMEMBRANE REDOX COMPLEX THROUGH
-I- FUNCTION: ARE TRANSFERRED TO THE CYTOPLASM FOR REDUCTION OF
  METAL
BINDING
                                                                                                                                          SIGNAL
                                                                                                                                                                                              InterPro; IPR002322; Cyt_CIII.
InterPro; IPR000345; CytC_heme_BS.
IPfam; PF02085; Cytochrome_CIII; 1.
PRINTS; PR00609; CYTOCHROMEC3.
PROSITE; PS00190; CYTOCHROME_C; 9.
                                                                                                                                                                                                                                                                                                    EMBL; AP186393; AAD56586.1; -. PIR; JC7094; JC7094. PDB; 19HC; 01-DEC-99.
                                                                                                                                                                                                                                                                                                                                                                                                                        This SWISS-PROT entry is copyright. It is produced through between the Swiss Institute of Bioinformatics and the Enthe European Bioinformatics Institute. There are no restruse by non-profit institutions as long as its content modified and this statement is not removed. Usage by and
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                                                                                                                         METAL
                                                                                                                                                                                                                                                                                                                                                                                  entities requires a license agreement (S or send an email to license@isb-sib.ch).
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               STRAIN=ATCC
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        MEDLINE=99148120; PubMed=10368280;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             and modelling studies of its interaction
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    primary sequence
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  SEQUENCE FROM N.A., AND X-RAY CRYSTALLOGRAPHY (1.8 ANGSTROMS) STRAIN=ATCC 27774;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          MEDLINE=99400423; PubMed=10471375;
Saraiva L.M., da Costa P.N., LeGall J.;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Bacteria; Proteobacteria; Deltaproteobacteria; Desulfovibrionales; Desulfovibrionaceae; Desulfovibrio.
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16-OCT-2001 (Rel.
28-FEB-2003 (Rel.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            K-RAY CRYSTALLOGRAPHY (1.8 ANGSTROMS).
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Biochem. Biophys. Res. Commun. 262:629-634(1999).
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SUBLUIT: MONOMER.
SUBURIT: MONOMER.
SUBCELLULAR LOCATION: Periplasmic.
SUBCELLULAR LOCATION: Periplasmic.
PTM: BINDS 9 HEME GROUPS. ARRANGED INTO TWO TETRAHEME CLUSTERS
THE EXTRA HEME 4 IS LOCATED ASYMMETRICALLY BETWEEN THE TWO
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Biol. Inorg. Chem. 4:478-494(1999).
                                                                                                                                                                                   transport;
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Last annotation update)
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                                                          SWEH
                                                                                                  IRON
                                                                                                                                          NINE-HEME
                  IRON
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                                                      E-HEME CYTOCHROME C.

W (HEME 1 AXIAL LIGAND).

W (HEME 3 AXIAL LIGAND).

E 1 (COVALENT).

E 1 (COVALENT).
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(COVALENT)
                                                                                                                                                                                                                                                                                                                                                                                                     (See http://www.isb-sib.ch/announce/
                                                                                                                                                                             Signal; Repeat; 3D-structure.
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                LIGAND)
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